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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,959	06/30/2006	Yossi Shevach	298856-00003 (237876)	3083

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EXAMINER	
ML, QIUWEN	

ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
06/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipmail@eckertseamans.com

Office Action Summary	Application No.	Applicant(s)	
	10/596,959	SHEVACH, YOSSI	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-8,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-12 are pending.

Applicant's election of Group III, claims 9 and 10, in the reply filed on 2/26/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-8, 11, and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 9 and 10 are examined on the merits.

Claim Objections

Claims 9 and 10 are objected to because of the following informalities: Claim 9 recites "dry astragalus membranaceus extract" (line 5), and Claim 10 recites "dry withania somniferum extract" (line 5). Applicant is reminded that Latin name should be written in the proper format, wherein the first word is capitalized, the second word is lowercase and the entire name is italicized. Therefore, "*Astragalus membranaceus*", and "*Withania somniferum*" should be the correct recitations.

Specification Objections

The disclosure is objected to because of the following informalities: The specification recites "novel" on page 7. It is suggested that the term "novel" be deleted from the language of the specification. Once the determination of the novelty of a claimed invention has been established and the disclosure of the invention made public and/or patented, the claimed invention is no longer novel or new, since the scope of the invention no longer embraces what is considered "novel". Thus, the incorporation of the term "novel" into the language of the specification is not appropriate. Correction is required.

Claim Rejections –35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 recite the limitation "the blood count" in line 1. There is insufficient antecedent basis for this limitation in the claim. There are different types of cells in the blood, such as white blood cells (leukocytes), red blood cells (erythrocytes), and platelets (thrombocytes), and it is not clear what blood (cell) count Applicant is referring to.

Therefore, the metes and bounds of claims are rendered vague and indefinite. The lack of clarity renders the claims very confusing and ambiguous since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ha et al (Ha et al, A laboratory study on *Astragalus membranaceus* mistura in the prophylaxis and treatment of myelosuppression caused by cancer chemotherapy, Journal of China Medical University, (Oct., 1997) Vol. 26, No. 5, pp. 449-452, 462) in view of Ghosh et al (Ghosh et al, Physiological potential of bata-carotene in prolonging the survival of the host bearing transplatable murine lymphoma, Planta Med 61 (1995) 317-320).

Ha et al evaluate the effect of *Astragalus membranaceus* mistura on the chemotherapy-associated toxicity (see Abstract). *Astragalus membranaceus* was administered orally to tumor bearing mouse (see page 3, 1st paragraph of the full translation). It was shown that the leukocyte and platelet counts were much more in the group treated with *Astragalus membranaceus* (thus a method of increasing the blood count of a subject, especially a subject going through a chemotherapy treatment) ($P < 0.01$); the macrophage phagocytotic ability and lymphocyte transformation percentage were significantly higher in the group treated with *Astragalus membranaceus* ($P < 0.01$). It was concluded that *Astragalus membranaceus* mistura could overcome the toxicity of cancer chemotherapy in hematopoietic system. This therapy was effective in modulating myelosuppression induced by chemotherapy. *Astragalus membranaceus*

mistura was effective for the enhancement of cellular immune response, and was able to improve the function of both lymphocytes and macrophages. *Astragalus membranaceus* mistura could protect reticulocyte and monocyte-macrophage from impairment caused by chemotherapy (see Abstract, full translation is attached).

Ha et al do not teach the incorporation of dry beet extract into the composition, neither do Ha et al teach using dry *Astragalus membranaceus* extract.

Ghosh et al teach supplementation of beta-carotene (BC) before tumor inoculation caused an 1.6-fold increase in survival. Survival was also favorably influenced by the carrot and beet though to a lesser degree than pure BC (page 318, 3rd paragraph). Carrot and beet extracts (the same as red beet extract) were given as the only source of water (thus orally administration) starting 15 days prior to tumor inoculation and continued throughout the experiment (page 318, 2nd column, Fig. 2). A slow reversal of lymphoid myeloid ratio and high normal hemoglobin (Hb) level was observed in BC treated animals (thus a method of increasing blood count) (page 318, 2nd column, 2nd paragraph). Ghosh et al also teach BC is known to inhibit red blood cell hemolysis induced by cholesterol hydroperoxide and the high hemoglobin has inhibitory influence on tumor growth. The increase in total leucocyte count and appearance of many forms of abnormal and aberrant neutrophilis and a slow reversal of the lymphoid myeloid ratio in the last phase of survival in experimental groups suggests definite contribution of BC in controlling these factors (page 319, 2nd column, last paragraph).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to incorporate the beet extract from Ghosh et al since Ghosh et al teach the beet extract increased the survival rate of tumor bearing mice, and also increase the hemoglobin

level and total leucocyte count (thus increasing the blood count) in the treatment group. Therefore, it would have obvious to combine beet extract with *Astragalus membranaceus* extract in the chemotherapy treatment to increase the survival rate of the patient and increase the blood count and myelosuppression induced by chemotherapy. Since both Ha et al and Ghosh et al provide evidence for increasing blood count in chemotherapy treatment using *Astragalus membranaceus* extract, and beet extract, respectively, one of ordinary skill in the art would have been motivated to make the modifications to combine the teachings of two references together.

It would also have obvious to use dry red beet extract and dry *Astragalus membranaceus* extract since it is a conventional practice to feed mice with a liquid form of a drug through IG so as to quantify the drug intake. However, as to a human subject, solid (dry) forms of drugs such as tablets, capsules are more stable and convenient to the users. Regarding the limitation to the form of the extract, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, which is dependent on the stability and solubility of the drugs.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kapadi et al (WO 02/079748 A2), in view of Ghosh et al (Ghosh et al, Physiological potential of bata-

carotene in prolonging the survival of the host bearing transplatable murine lymphoma, Planta Med 61 (1995) 317-320).

Kapadi et al teach a composition useful for ameliorating or reversing naturally occurring immunosuppression or myelosuppressive, or side effects of myelosuppressive or immunosuppressive drug therapy. Medicinal fractions derived from the plant *Withania somnifera* that reverse, at least in part, one or more characteristics of immunosuppression or myelosuppression and a process for manufacturing the fractions are particular aspects of the invention. *Withania somnifera* medicinal fractions have additional biological activities including anti-tumor potentiating activity (see Abstract). Kapadi et al also teach the invention compositions have one or more of immune stimulating or anti-cell proliferative activity in a subject, the inventions also provides methods for stimulating an immune response (e.g., increasing the number of white blood cells) or anti-cell proliferative activity in a subject. In one embodiment, a method includes administering to a subject an amount of an invention composition effective to increase the number of white blood cells in the subject. In one aspect, the white blood cells are selected from monocytes, macrophages natural killer cells, dendritic cells, granulocytes, basophilis and oesinophils. In another aspect, the subject has less than normal numbers of white blood cells (page 6, last paragraph, bridging page 7). Kapadi et al further teach myelosuppression or immunosuppression may result directly or indirectly from anti-cell proliferative or anti-cancer (e.g., radiation, radioisotopes, chemotherapy, etc) (col 19, lines 20-25). Kapadi et al further teach administering about 50 mg/kg subject mass of the composition to a Balb-c mouse increases by about 20% or more the number of white blood cells in the Balb-c mouse (claim 31) (thus a method of increasing blood count of a subject) . Kapadi et al further teach the formulation

comprises a pill, granules, crystals, a capsule etc (thus dry *withania somniferum* extract, thus orally administering).

Kapadi et al do not teach the incorporation of dry beet extract into the composition.

Ghosh et al teach supplementation of beta-carotene (BC) before tumor inoculation caused an 1.6-fold increase in survival. Survival was also favorably influenced by the carrot and beet though to a lesser degree than pure BC (page 318, 3rd paragraph). Carrot and beet extracts were given as the only source of water starting 15 days prior to tumor inoculation and continued throughout the experiment (page 318, 2nd column, Fig. 2). A slow reversal of lymphoid myeloid ratio and high normal hemoglobin (Hb) level was observed in BC treated animals (thus a method of increasing blood count) (page 318, 2nd column, 2nd paragraph). Ghosh et al also teach BC is known to inhibit red blood cell hemolysis induced by cholesterol hydroperoxide and the high hemoglobin has inhibitory influence on tumor growth. The increase in total leucocyte count and appearance of many forms of abnormal and aberrant neutrophilis and a slow reversal of the lymphoid myeloid ratio in the last phase of survival in experimental groups suggests definite contribution of BC in controlling these factors (page 319, 2nd column, last paragraph).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to incorporate the beet extract from Ghosh et al since Ghosh et al teach the beet extract increased the survival rate of tumor bearing mice, and also increase the hemoglobin level and total leucocyte count (thus increasing the blood count) in the treatment group. Therefore, it would have obvious to combine beet extract with *Withania somnifera* extract in the chemotherapy treatment to increase the survival rate of the patient and increase the blood count and myelosuppression induced by chemotherapy. Since Kapadi et al and Ghosh et al provide

evidence for increasing blood count in chemotherapy treatment using *Withania somnifera* extract, and beet extract, respectively, one of ordinary skill in the art would have been motivated to make the modifications to combine the teachings of two references together.

It would also have obvious to use dry red beet extract since it is a conventional practice to feed mice with a liquid form of a drug through IG so as to quantify the drug intake. However, as to a human subject, solid (dry) forms of drugs such as tablets, capsules are more stable and convenient to the users. Regarding the limitation to the form of the extract, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, which is dependent on the stability and solubility of the drugs.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Examiner, Art Unit 1655